

**DOCKET NO.:** ISIS-4847  
**Application No.:** 09/965,551  
**Office Action Dated:** August 20, 2003

**PATENT**

### **REMARKS/ARGUMENTS**

Claims 28-30 and 52-69 are presently pending. As a preliminary matter, Applicant wishes to thank the Examiner for entering claims 52-69.

#### **I. Rejections Under 35 U.S.C. § 112, First Paragraph**

Claims 28-30 and 52-69 continue to stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. Applicant continues to traverse this rejection for all of the reasons of record, and respectfully requests reconsideration in view of two additional points.

First, Applicant wishes to apprise the Examiner of a press release dated September 10, 2003, in which Genta Incorporated announced results from its successful Phase 3 clinical trial in which the effects of the antisense drug Genasense™ against malignant melanoma were studied. (Exhibit A attached hereto) These results, along with the previously described clinical trials of antisense therapies of record, establish that antisense technology does work *in vivo* in accordance with the principles and guidance set forth in the present application. Accordingly, the Genasense™ results further refute the Examiner's allegations that antisense remains a highly unpredictable art.

Second, the Examiner has improperly relied upon a medical dictionary, rather than a standard dictionary, to determine the meaning of claim terms. Recently, the Federal Circuit in *E-pass Technologies, Inc. v. 3Com Corp.*, Fed. Cir., No. 02-1593, (August 20, 2003) determined that the meaning of patent terms that have a meaning in everyday usage do not turn on the manner in which it happens to be used in the context of a particular industry. The Federal Circuit held that the ordinary meaning of "card" in the claim term "electronic multi-function card" for a patent on simplifying the use of multiple credit cards did not require resort to standard size dimensions observed by the credit card industry. In its ruling, the Federal Circuit noted that the ordinary meaning of "card" given in Merriam-Webster's Collegiate Dictionary, Random House Webster's Unabridged Dictionary, and The Oxford English Dictionary provides no specific length, width, or depth measurements. In concluding that the district court's construction of the claim term "electronic multi-function card" requiring specific industry standard size dimensions was incorrect, the Federal Circuit noted

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that it "indulge[s] a 'heavy presumption' that a claim term carries its ordinary and customary meaning." *Sunrace Roots Enter. Co., LTD v. SRAM Corp.*, No. 02-1524, slip op. at 8 (Fed. Cir. July 17, 2003) (quoting *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002)).

In view of this legal authority, the Examiner's resort to medical dictionaries is improper. Here, the instant claims recite methods for **treating an organism** having a disease characterized by the undesired production of a protein [the preamble], comprising **contacting said organism** [the method step]. Despite Applicant's clear explanation of the ordinary and customary meaning of the claim term *treating*, the Examiner continues to improperly read into the claims medical terminology in alleging that the claim is not enabled. According to the Examiner:

"Despite Applicants repeated attempts to steer the emphasis of their claims toward the method step of contacting an organism, **the expressly claimed purpose of such contacting is for administering treatment**, which is not considered to be enabled."

Advisory Action at page 2, par. 2, line 4.

Notably, the claims are not drawn to "administering treatment", nor are they drawn "to care for medicinally or surgically; to manage in the use of remedies or appliances; as to treat a disease, a wound, or a patient", which the Examiner seems to inject into Applicant's claims using the medical definition of the word "treatment" from the CancerWeb website of medical terminology. **Indeed, the word "treatment" does not appear anywhere in Applicant's claims.** Instead, Applicant's ordinary and customary meaning of the term *treating* requires only the administration of a compound to an organism to satisfy the claimed "contacting" step. According to Merriam-Webster Online (Exhibit B), one meaning of the verb *to treat* is: "to act upon with some agent especially to improve or alter, *e.g.*, to treat a metal with acid. Also, Webster's II defines the verb *to treat* as: "to subject to an action, process or change." (Exhibit C). Applicant's claims are not drawn to "treating patients" as purported by the Examiner, but rather they are drawn to contacting an organism with one or more of the recited compounds to bring about a change in the undesired production of a protein. Thus, Applicant's use of the term *treating* is clear in view its ordinary and customary dictionary definition.

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Given that the claims require only a minimum of "contacting" and not, for example, "administering treatment", the only issue under 35 U.S.C. §112 is whether those skilled in the art having knowledge of Applicant's disclosure would require undue experimentation in performing the claimed step of "contacting." For the reasons already of record, Applicant respectfully maintains that one skilled in the art would not require undue experimentation in performing the claimed step of "contacting." And given a proper comparison of the claim language to the teaching of the specification, Applicant submits that the pending claims are fully enabled, and requests that the Examiner withdraw the rejections under 35 U.S.C. section 112.

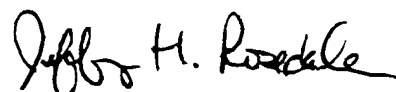
**Conclusions:**

Applicant requests the Examiner to:

- (1) reconsider and withdraw the rejection of the claims; and
- (2) pass claims 28-30 and 52-69 to allowance.

If the Examiner is of contrary view, the Examiner is requested to contact the undersigned attorney at 215-568-3100.

Date: October 7, 2003



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**EXHIBIT A****Genta and Aventis Report Positive Results in Phase 3 Trial of Genasense™ Plus Chemotherapy in Patients with Advanced Malignant Melanoma*****NDA Submission to the FDA Initiated***

**BERKELEY HEIGHTS and STRASBOURG, FRANCE – September 10, 2003** —Genta Incorporated (Nasdaq: GNTA) and Aventis (NYSE:AVE) today announced results from their Phase 3 clinical study of Genasense™ (oblimersen sodium) plus chemotherapy in patients with malignant melanoma. In conjunction with these results, the first portion of the New Drug Application (NDA) has been submitted to the Food and Drug Administration (FDA) for Genasense in this indication.

Senior executives from Genta and Aventis will discuss results of the study on a conference call that will be webcast beginning at 8:00 a.m. EST on Wednesday, September 10, 2003.

The Phase 3 trial enrolled patients at 140 sites from 12 different countries. A total of 771 chemotherapy naive patients were randomly assigned to receive dacarbazine (a standard chemotherapy drug) alone or in combination with Genasense. The primary endpoint of this trial was to compare the overall survival between the two treatment arms. Secondary endpoints included comparative analyses of progression-free survival and tumor response. The following results were obtained:

- Analysis of all patients on an intent-to-treat (ITT) basis showed that the addition of Genasense to dacarbazine resulted in a median survival of 9.1 months, compared with 7.9 months for patients treated with dacarbazine alone ( $P=0.184$ ).
- For patients treated per-protocol who have completed a minimum follow-up of 12 months ( $N=480$ ), the addition of Genasense resulted in a median survival of 10.1 months, compared with 8.1 months for dacarbazine alone ( $P=0.035$ ).
- For the ITT population ( $n=771$ ), patients treated with Genasense plus dacarbazine showed a significant increase in median progression-free survival to 78 days, compared with 49 days for patients treated with dacarbazine alone ( $P=0.001$ ).
- For the ITT population ( $n=771$ ), patients treated with Genasense plus dacarbazine achieved an antitumor response rate of 11.7% (using RECIST criteria), compared with 6.8% for patients treated with dacarbazine alone ( $P=0.019$ ).
- The addition of Genasense to dacarbazine did not appear to be associated with serious, previously unreported adverse reactions compared with the use of dacarbazine alone.

"Metastatic melanoma is one of the most devastating forms of cancer," said Loretta M. Itri, MD Genta's President, Pharmaceutical Development, and Chief Medical Officer. "These results have been observed in a disease that is notoriously unresponsive to standard therapy and for which no approved drug has shown a survival advantage. We believe the current data support the NDA submission we have initiated using provisions granted under the "Fast Track" designation for Genasense."

"One of our primary goals at Aventis is to deliver innovative products that help patients with cancer live longer with a better quality of life. Today's promising data may lead to an important advance in targeted therapies for patients with advanced malignant melanoma," said Frank Douglas, M.D., head of Drug Innovation and Approval, and Member of the Board of Management at Aventis. "Our collaboration with Genta to develop and co-market Genasense underscores our commitment to develop breakthrough late-stage compounds that have significant benefit for patients as well as commercial potential."

"Genasense may significantly impact the way in which we treat metastatic melanoma," stated Frank Haluska, MD, PhD, Director of the Melanoma Program at Massachusetts General Hospital, and Assistant Professor of Medicine, Harvard Medical School. "The improvement shown in this very large trial marks a critical step in using targeted molecular approaches to attack this life-threatening disease."

The results from this trial will be presented at an upcoming scientific meeting this Fall.

A live conference call can be accessed as follows:  
U.S./Canada: Dial (877) 634-8606, reference code: 2741947.

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International: Dial (706) 679-3140, reference code: 2741947.

A replay will be available two hours after the completion of the conference call and archived through Friday, October 10, 2003, accessible as follows:

U.S./Canada: Dial (800) 642-1687, enter 2741947 for conference ID.

International: Dial (706) 645-9291, enter 2741947 for conference ID.

The audio webcast can also be accessed via the web at Genta's Investor Relations website at: <http://www.genta.com/genta/InvestorRelation/events.htm> and will be archived for 30 days.

#### **About Genasense**

Genasense is the first oncology drug of its kind to directly target the biochemical pathway (known as apoptosis) whereby cancer cells are ultimately killed by chemotherapy. Genasense is believed to inhibit the production of Bcl-2, a protein that is highly expressed in malignant melanoma and that is believed to be a fundamental cause of resistance to anticancer therapy. By inhibiting Bcl-2, Genasense may greatly improve the activity of anticancer therapy.

Genasense, which is being developed in collaboration with Aventis, is currently the subject of 20 clinical studies, including randomized trials in patients with prostate cancer, small cell lung cancer, and non-small cell lung cancer. Additional non-randomized trials are ongoing for patients with myeloma, non-Hodgkin's lymphoma (NHL), acute myeloid leukemia, mantle cell lymphoma, and cancers of the breast, lung, colon, prostate, stomach, pancreas, liver and kidney.

#### **About Melanoma**

Malignant melanoma is the most deadly form of skin cancer. The incidence of this disease is increasing by approximately 4% annually in the US. In 2002, almost 54,000 cases of malignant melanoma were diagnosed. Melanoma is the number one cause of cancer death in women aged 25 to 30. For more information on melanoma please visit :

[http://www.nci.nih.gov/cancer\\_information/cancer\\_type/melanoma](http://www.nci.nih.gov/cancer_information/cancer_type/melanoma)

#### **About Genta**

Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on delivering innovative products for the treatment of patients with cancer. The Company's research platform is anchored by two major programs that center on RNA/DNA-based medicines and small molecules. Genasense™ (oblimersen sodium), the Company's lead compound from its RNA/DNA Medicines program, is being developed with Aventis and is currently undergoing late-stage, Phase 3 clinical testing. The leading drug in Genta's small molecule program is Ganite™ (gallium nitrate injection), which the Company intends to market for the treatment of cancer-related hypercalcemia that is resistant to hydration. For more information about Genta, please visit our website at: [www.genta.com](http://www.genta.com).

#### **About Aventis**

Aventis is dedicated to treating and preventing disease by discovering and developing innovative prescription drugs and human vaccines. In 2002, Aventis generated sales of € 17.6 billion, invested € 3.1 billion in research and development and employed approximately 71,000 people in its core business. Aventis corporate headquarters are in Strasbourg, France. For more information, please visit: [www.aventis.com](http://www.aventis.com)

*This press release and the associated conference call contain forward-looking statements with respect to business conducted by Genta Incorporated and Aventis Incorporated. By their nature, forward-looking statements and forecasts involve risks and uncertainties because they relate to events and depend on circumstances that will occur in the future. There are a number of factors that could cause actual results and developments to differ materially. For a discussion of those risks and uncertainties, please see the Companies' Annual Report/Form 10-K for 2002.*

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## EXHIBIT B

Merriam-Webster Online: <http://www.m-w.com/cgi-bin/dictionary>

Main Entry: **'treat** ˈtri:t

Pronunciation: 'tri:t

Function: *verb*

Etymology: Middle English *treten*, from Old French *traitier*, from Latin *tractare* to drag about, handle, deal with, frequentative of *trahere* to drag, pull

Date: 14th century

*intransitive senses*

1 : to discuss terms of accommodation or settlement : **NEGOTIATE**

2 : to deal with a matter especially in writing : **DISCOURSE** -- usually used with *of* <a book *treating* of conservation>

3 : to pay another's expenses (as for a meal or drink) especially as a compliment or as an expression of regard or friendship

*transitive senses*

1 a : to deal with in speech or writing : **EXPOUND** b : to present or represent artistically c : to deal with : **HANDLE** <food is plentiful and *treated* with imagination -- Cecil Beaton>

2 a : to bear oneself toward : **USE** <*treat* a horse cruelly> b : to regard and deal with in a specified manner -- usually used with *as*

3 a : to provide with free food, drink, or entertainment b : to provide with enjoyment or gratification

4 : to care for or deal with medically or surgically <*treat* a disease>

5 : to act upon with some agent especially to improve or alter <*treat* a metal with acid>

- **treat-er** *noun*

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**EXHIBIT C**



**Webster's II**  

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*New College Dictionary*

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## EXHIBIT C

Words are included in this Dictionary on the basis of their usage. Words that are known to have current trademark registrations are shown with an initial capital and are also identified as trademarks. No investigation has been made of common-law trademark rights in any word, because such investigation is impracticable. The inclusion of any word in this Dictionary is not, however, an expression of the Publisher's opinion as to whether or not it is subject to proprietary rights. Indeed, no definition in this Dictionary is to be regarded as affecting the validity of any trademark.

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## EXHIBIT C

**treat** (trēt) *v.* **treat-ed, treat-ing, treats.** [ME *treten* < AN *tratan* < Lat. *tractare*, freq. of *trahere*, to draw.] — *vt.* 1. To have to do with or behave in a specified manner toward <*treat* all employees fairly> 2. To consider or regard in a certain way <*treated* me as a member of the family> 3. To deal with in speech or writing <an article *treating* English antiques> 4. To represent or deal with in a specified style or manner, as in art or literature <*treat* a subject allegorically> 5. To entertain (another) at one's own expense <*treated* me to dinner> 6. To subject to an action, process, or change, esp.: a. To give medical aid to <*treat* sick patients> b. To subject to a chemical or physical process or application. — *vi.* 1. To deal with a subject or topic in speech, writing, or thought <The essay *treats* of medieval chivalry.> 2. To pay for another's entertainment or food. 3. To negotiate : bargain. — *n.* 1. Something, as one's food or entertainment, paid for by another person. 2. Provision of a treat, esp. in return for something else. 3. A special delight <A trip to Paris was a real *treat*.> — **treat'-a-ble** *adj.* — **treat'-er** *n.*